Treatment with a Green Tea Polyphenol Corrects Craniofacial Deficits Associated with Down Syndrome

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Down syndrome (DS) is caused by trisomy of human chromosome 21 (HSA21). Individuals with DS present craniofacial abnormalities including an undersized, dismorphic mandible leading to difficulty with eating, breathing, and swallowing. Using the Ts65Dn DS mouse model (three copies of ~50% HSA21 homologs), we have traced the mandibular deficit to a neural crest cell (NCC) deficiency and reduction in first pharyngeal arch (PA1 or mandibular precursor) size at embryonic day 9.5. At E9.5, Dyrk1A, a triplicated DS candidate gene, is overexpressed and may cause the NCC and PA1 deficits. We hypothesize that treatment of pregnant Ts65Dn mothers with Epigallocatechin gallate (EGCG), a known Dyrk1A inhibitor, will correct NCC deficits and rescue the undersized PA1 in trisomic E9.5 embryos. To test our hypothesis, we treated pregnant Ts65Dn mothers with EGCG from either E7-E8 or E0-E9.5. Our preliminary study found an increase in PA1 volume and NCC number in trisomic E9.5 embryos after treatment, but observed differences between treatment regimens. Differential gene expression was also quantified in trisomic treated embryos. This preliminary data suggests EGCG treatment has the potential to rescue the mandibular phenotype caused by trisomy. These findings provide preclinical testing for a potential therapy for craniofacial disorders linked to DS.

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